wherein X_1 and X_3 may be the same or different and each is an amino acid sequence consisting of from 0 to 40 naturally occurring amino acid residues; X_2 is any amino acid sequence of from 10 to 15 residues derived from or contiguous within amino acids 506 to 518 inclusive of human GAD65 or amino acids 24 to 36 inclusive or derivatives thereof of human proinsulin; and wherein said peptide is capable of reacting with T cells and modifying T-cell function when incubated with cells from subjects with pre-clinical or clinical Insulin-Dependent Diabetes Mellitus (IDDM).

43. (Amended) A method of treatment comprising administering to a subject an effective amount of a peptide for a time and under conditions sufficient to remove or substantially reduce the presence in said subject of autoreactive T-cells or autoantibodies to IDDM autoantigens wherein the peptide consists of the formula:

$X_1X_2X_3$

wherein X_1 and X_3 may be the same or different and each is an amino acid sequence consisting of from 0 to 40 naturally occurring amino acid residues; X_2 is selected from FFYTPKTRREAED (SEQ ID NO:1) and FWYIPPSLRTLED (SEQ ID NO:2) and wherein said peptide is capable of reacting with T cells and modifying T-cell function when incubated with cells from subjects having pre-clinical or clinical IDDM.

REMARKS

In the Official Action dated February 21, 2001, Claims 39, 40, 42 and 43 have been rejected under 35 U.S.C. §112, first paragraph as allegedly lacking descriptive support. Claims 39, 40, 42 and 43 have also been rejected under 35 U.S.C. §112, first paragraph as allegedly lacking enabling support.

In response, applicants have amended the claims, which when accompanied by the foregoing amendments is deemed to place the present application in condition for allowance. Favorable consideration of all pending claims is therefore respectfully requested.

Claims 39, 40, 42 and 43 have been rejected under 35 U.S.C. §112, first paragraph as allegedly lacking descriptive support. The Examiner specifically alleges that claims drawn to "homologous" sequences, "derivatives", or "chemical equivalents" of the disclosed GAD65 or proinsulin sequences lack support in the description of the specification, as filed.

Applicants respectfully direct the Examiner's attention to the specification at Figure 1 wherein the specification adequately conveys to the skilled artisan, with reasonable clarity, homologs of SEQ ID NOS:1 and 2, consistent with Fiers v. Revel, 25 USPQ2d 1601 (Fed. Cir. 1993) and Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016 (Fed Cir. 1991). Notably, the specification provides the sequences of mouse proinsulin 1 (24-36; SEQ ID NO:3); mouse proinsulin 2 (24-36; SEQ ID NO:4); mouse GAD 65 (506-508; SEQ ID NO:5); human GAD 67 (515-527; SEQ ID NO:6); and mouse GAD 67 (514-526; SEQ ID NO:7). Applicants submit that the foregoing sequences constitute a "representative number" of molecules falling within the scope of the claimed genus-homologs of human GAD 65. However, in an effort to expedite favorable prosecution on the merits, applicants have deleted the recitations "homologous sequences", "derivatives" or "chemical equivalents" from the pending claims.

The Examiner has also alleged that Claims 39, 40, 42 and 43 lack enabling support pursuant to 35 U.S.C. §112, first paragraph. The Examiner specifically alleges that the claims are drawn to, inter alia, "non-naturally occurring" amino acid residues. Notably,

applicants respectfully direct the Examiner's attention to Page 6, lines 10-14 wherein several examples of non-natural amino acids (termed "unnatural" amino acids) are provided.

The Examiner further alleges that the practitioner is "not provided with any guidance regarding the manufacture of homologous sequences...." Applicants respectfully submit that the specification explicitly provides homologs of SEQ ID NOS:1 and 2 in Figure 1. The five homologs are commonly synthesized by methods well within the ken of the ordinarily skilled artisan (see e.g., Pages 3, line 30 – Page 4, line 12). Accordingly, the provided homologs taken with the T-cell proliferative responses reported at Example 4 of the specification, leads to the inescapable conclusion that the present application not only describes homologs of SEQ ID NOS:1 and 2, but also enables immunogenic and functional properties associated with such homologs. Inasmuch as the application clearly provides the data and descriptive support for homologous sequences of SEQ ID NOS:1 and 2, applicants specifically reserve the right to file one or more continuing applications directed to subject matter encompassing homologs of SEQ ID NOS:1 and 2. Nevertheless, in an effort to expedite favorable prosecution, applicants have deleted the recitation "homologous sequences", "derivatives", "chemical equivalents" and "non-naturally occurring amino acid residues" from all pending claims.

Accordingly, the rejection of Claims 39, 40, 42 and 43 under 35 U.S.C. §112, first paragraph is overcome and withdrawal thereof is respectfully requested.

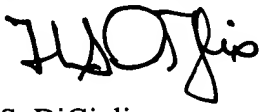
Applicants have amended Claims 39, 40, 42 and 43 to further define the subject matter to which applicants are entitled. Specifically, the Claims have been amended to recite a recombinant or synthetic peptide consisting of the formula $X_1X_2X_3$ wherein X_1 and X_3 may be the same or different and each is an amino acid sequence consisting of 0 to 40 naturally occurring

amino acid residues. Support for the recitation "0 to 40 naturally occurring amino acid residues" is found throughout the specification and particularly at Page 2, line 26; Page 7, line 13; and Page 9, line 27. No new matter has been added.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "Version with markings to show changes made".

Accordingly, in view of the foregoing amendments and remarks, the present application is deemed to be in condition for allowance which action is earnestly solicited.

Respectfully submitted,



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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS:

39. (Amended) A recombinant or synthetic peptide [or chemical equivalent thereof] consisting of the formula:

$$X_1 X_2 X_3$$

wherein X_1 and X_3 may be the same or different and each is an amino acid sequence consisting of from [0 to 15] 0 to 40 naturally [or non-naturally] occurring amino acid residues; X_2 is any amino acid sequence of from 10 to 15 residues derived from[, homologous to] or contiguous within amino acids 506 to 518 inclusive [or derivatives thereof] of human GAD65 or amino acids 24 to 36 inclusive [or derivatives thereof] of human proinsulin; and wherein said peptide [or chemical equivalent thereof] is capable of reacting with T cells and modifying T-cell function when incubated with cells from subjects with pre-clinical or clinical Insulin-Dependent Diabetes Mellitus (IDDM).

40. (Amended) A recombinant or synthetic peptide [or chemical equivalent thereof] consisting of the sequence:

$$X_1 X_2 X_3$$

wherein X_1 and X_3 may be the same or different and each is an amino acid sequence consisting of from [0 to 15] 0 to 40 naturally [or non-naturally] occurring amino acid residues; X_2 is selected from FFYTPKTRREAED (SEQ ID NO:1) and FWYIPPSLRTLED (SEQ ID NO:2) [or a derivative or chemical equivalent thereof] and wherein said peptide is capable of reacting with

T cells and modifying T-cell function when incubated with cells from subjects having pre-clinical or clinical IDDM.

42. (Amended) A method of treatment comprising administering to a subject an effective amount of a peptide [or chemical equivalent thereof] for a time and under conditions sufficient to remove or substantially reduce the presence in said subject of autoreactive T-cells [and/or] or autoantibodies to IDDM autoantigens wherein the peptide consists of the formula:

$$X_1 X_2 X_3$$

wherein X_1 and X_3 may be the same or different and each is an amino acid sequence consisting of from [0 to 15] 0 to 40 naturally [or non-naturally] occurring amino acid residues; X_2 is any amino acid sequence of from 10 to 15 residues derived from[, homologous to] or contiguous within amino acids 506 to 518 inclusive [or derivatives thereof] of human GAD65 or amino acids 24 to 36 inclusive or derivatives thereof of human proinsulin; and wherein said peptide [or chemical equivalent thereof] is capable of reacting with T cells and modifying T-cell function when incubated with cells from subjects with pre-clinical or clinical Insulin-Dependent Diabetes Mellitus (IDDM).

43. (Amended) A method of treatment comprising administering to a subject an effective amount of a peptide [or chemical equivalent thereof] for a time and under conditions sufficient to remove or substantially reduce the presence in said subject of autoreactive T-cells [and/or] or autoantibodies to IDDM autoantigens wherein the peptide consists of the formula:

$$X_1X_2X_3$$

wherein X_1 and X_3 may be the same or different and each is an amino acid sequence consisting of from [0 to 15] 0 to 40 naturally [or non-naturally] occurring amino acid residues; X_2 is selected

from FFYTPKTRREAED (SEQ ID NO:1) and FWYIPPSLRTLED (SEQ ID NO:2) [or a derivative or chemical equivalent thereof] and wherein said peptide is capable of reacting with T cells and modifying T-cell function when incubated with cells from subjects having pre-clinical or clinical IDDM.